BARORECEPTOR-MEDIATED RESPONSES IN LEFT VENTRICULAR DYSFUNCTION FOLLOWING ACUTE MYOCARDIAL INFARCTION.

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Baroreceptor-mediated vasoconstrictor responses are impaired in patients with CHF and it has been suggested that abnormalities of this reflex early in LV dysfunction may be important in the development of increased sympathetic tone. We studied 24 patients (61±2yrs) within 2 weeks of an MI with no history of CHF but with an LVEF of ≤ 40% (34±1%). None had LVF at time of study or were on digoxin or ACE inhibitors. Other drugs were held on the study morning and lower body negative pressure (LBNP) was applied for 20 mins at -10 then -40 mmHg. Forearm vascular resistance (FVR) and hormones were measured and compared with 8 normals (53±4yrs). Mean ± s.e. *p<0.05 vs normals.

	NORMALS			MI		
	Pre	-10	-40	Pre	-10	-40
MBP mmHg	99±2	95±2	91±5	89±2*	89±2*	82±3
RAP mmHg	6.1±1	7.1±1	2.3±0.8	6.3±1.1	4.6±1.1	1.4±0.9
FVR units	50±7	53±8	81±17	47±4	53±5	63±6
NE pg/ml	177±38	175±22	341±4	230±25	345±36	422±41
R ng/ml/hr	1.0±0.1	0.8±0.1	1.1±0.1	2.8±0.5*	3.0±0.6*	4.9±1.2*
ANF pg/ml	20±4	20±4	12±4	92±20*	83±21*	70±15*
AVP pg/ml	0.6±0.1	0.6±0.1	1.4±0.5	3.6±1.5*	3.5±1.8*	16.7±8.3*

Thus, patients with a recent MI and significant LV dysfunction had elevated hormones at rest. In response to LBNP -40 mmHg they showed a normal forearm vasoconstrictor response, but a markedly abnormal elevation in AVP. This excessive vasoconstrictor hormone release implies increased sensitivity of the response and could be important in the development of CHF in some patients.

INTRINSIC ABNORMALITIES OF SKELETAL MUSCLE IN PATIENTS WITH CHRONIC HEART FAILURE: RELATION TO BLOOD FLOW

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Recent ultrastructural, biochemical and NMR-spectroscopy data demonstrated intrinsic abnormalities in skeletal muscle of patients with chronic heart failure; however, no relationship between abnormalities of skeletal muscle in the forearm (as measured by NMR spectroscopy) and blood flow as determined by plethysmography was observed (or suggested by measurements during ischemia). To evaluate the potential role of supplying blood flow (and oxygen delivery) in larger muscle masses (quantitative morphometry; needle biopsy of m. vastus lateralis) in ten patients with moderate to severe chronic heart failure (CHF, VO2 max 10-18 ml/kg/min). The volume density (Vvm) and the surface density of cristae (Svmc; ultrastructural correlate for oxydative metabolism) of mitochondria were significantly reduced in CHF compared to normals (VO2 max › 30 ml/kg/min) indicating reduced oxydative capacity of working muscle in patients with CHF. Femoral blood flow was measured during bicycle exercise by thermodilution (5 F catheter in the v. femoralis) ranging from 0.63 to 2.06 l/min/m². Maximal femoral flow during exercise correlated with Vvm (r = 0.579) and less closely with Svmc (r = 0.443) in these patients. Maximal cardiac index during exercise was significantly reduced in these patients with CHF (4.7 ± 0.6 l/min/m²).
Thus, chronically reduced femoral blood flow during physical activity may be an important factor contributing to the intrinsic abnormalities of skeletal muscle in patients with chronic heart failure.

LEFT VENTRICULAR REMODELLING IN THE COURSE OF EVOLVING HEART FAILURE.

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The time course of LV shape changes (ventricular remodelling) and associated hemodynamics were examined in 10 dogs with progressive global LV dysfunction leading to failure. Global LV dysfunction was produced by multiple sequential intracoronary embolizations with microspheres (average of 6 embolizations in 17 weeks). LV shape changes were quantitated from serial ventriculograms based upon the ratio of the major to minor axis at end-systole (ESR) and at end-diastole (EDR). Simultaneous measurements of LV ejection fraction (EF, %), LVEDP (mm Hg) and stroke volume (SV, ml) are shown in the table (mean ± SEM).

Weeks	0	2-5	7-10	12-15	17-20	22-33
ESR*	2.0±.12	1.7±.05	1.5±.04	1.5±.05	1.5±.06	1.4±.04
EDR*	1.5±.03	1.4±.04	1.3±.03	1.3±.03	1.2±.03	1.3±.03
EF*	64±2	47±2	43±3	36±4	30±4	23±2
LVEDP*	6±1	16±2	18±2	18±1	16±1	14±1
SV	41±4	—	38±4	36±5	36±4	33±5

(* indicates significant changes with time, P<.01)

The data indicate that as LV dysfunction progressed, the LV cavity changed from an ellipsoid to a nearly spherical shape. Remodelling occurred early and did not mirror the continued reduction of EF during the later stages of LV failure. This adaptation appears to maintain SV in the face of a continuing decline of LV function. Because of its early onset, LV remodelling may represent an early marker of impending LV failure.

Low angiotensinogen levels as an index of severity in heart failure. Consequence for renin measurement.

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To assess the status of renin-angiotensin system (RAS) in congestive heart failure (CHF), plasma renin activity (PRA, ngAI/ml/h), angiotensinogen (AG, ngAI/ml) and plasma active renin (AR, IRMA using monoclonal antibodies, pg/ml), were measured in 34 patients with CHF, 27 in NYHA Class II-III and 7 in class IV. Natremia (Na, mmol/l) and prealbumin (pAlb, mg/l) were measured to reflect the degree of water imbalance and liver dysfunction respectively.

NYHA	PRA	AR	AG	Na	pAlb
II-III	7.2±5.3	130±96	1204±353	137±3	260±55
IV	24.6±18.1**	655±740*	654±171*	129±4**	142±70**

(*p<0.0005 ; **p<0.0001 compared to Class II-III ; Mean value ± SD)

Patients with class IV showed lower levels of AG, pAlb, Na and higher levels of AR and PRA than those with class II-III (Table). AG levels were highly significantly correlated with AR (r = 0.46, p<0.005), PRA (r = 0.43, p<0.01), Na (r = 0.52, p<0.001) and pAlb (r = 0.49, p<0.001). The slope of the regression line of AR = f(PRA) was steeper for patients (n = 17) with AG ≤ 1100 ng/ml than for those (n = 17) with AG > 1100 ng/ml (respectively 17.1 and 11.7, p <0.005) indicating underestimation of PRA in low AG patients. AG is therefore an important parameter to consider in assessing the activity of the RAS in CHF patients. In patients with liver dysfunction, the decrease in AG leads to an underestimation of AR levels by PRA. Thus, direct IRMA of AR is a more reliable indicator of RAS activation in CHF.